Orthostatic Hypotension and Orthostatic Tachycardia

New Clinical Observations, Successful Treatment with Paredrine, and Review of Literature

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BRADBURY AND EGGLESTON[4] in 1925 first described orthostatic hypotension and since then relatively few reports have been recorded in the literature. Orthostatic hypotension is characterized chiefly by a sudden, sharp decrease in blood pressure when the afflicted patient assumes the upright position; and when the blood pressure reaches a low level, weakness and syncope result. The characteristic signs and symptoms are faintness, weakness, dimness of vision, severe headache, arrhythmias and syncope. When the patient assumes the erect position, especially after arising in the morning, or after exertion or fatigue, deficient perspiration, localized or generalized, and impaired renal function or oliguria may occur. Intolerance to heat, especially during the summer, impotence, and a positive reaction to the Flack[11] test are usually present. The blood pressure when the patient is supine is usually normal but in the standing position the systolic blood pressure may fall below 50-60 mm. of mercury. Faintness, dizziness, or syncope may follow. If a patient has exhaustion in the morning which decreases during the day, or dimness of vision or syncope which occurs on assumption of the erect position and disappears when supine, or if there are episodes of diminished sweating or of syncope inadequately explained, orthostatic hypotension should be suspected. The occurrence of orthostatic tachycardia with orthostatic hypotension has been often observed.

This condition has been considered by some to be the result of failure of adequate constriction of arterioles or a defect in the function of the sympathetic nervous system when the patient stands. Many observers[3, 6, 24] have emphasized the relationship between orthostatic hypotension and disease of the nervous system. Others[2, 5, 9, 15, 19, 20, 23, 26, 27, 31] have confirmed these observations and interpretations and have also advanced the possibility of the essential lesion in the hypothalamic region subserving the autonomic functions. Still others[1, 25] have emphasized the syndrome on the basis of disease of the peripheral autonomic nerves. It has been demonstrated repeatedly that this syndrome may occur in cases in which no disease of the nervous system could be discovered by clinical means.

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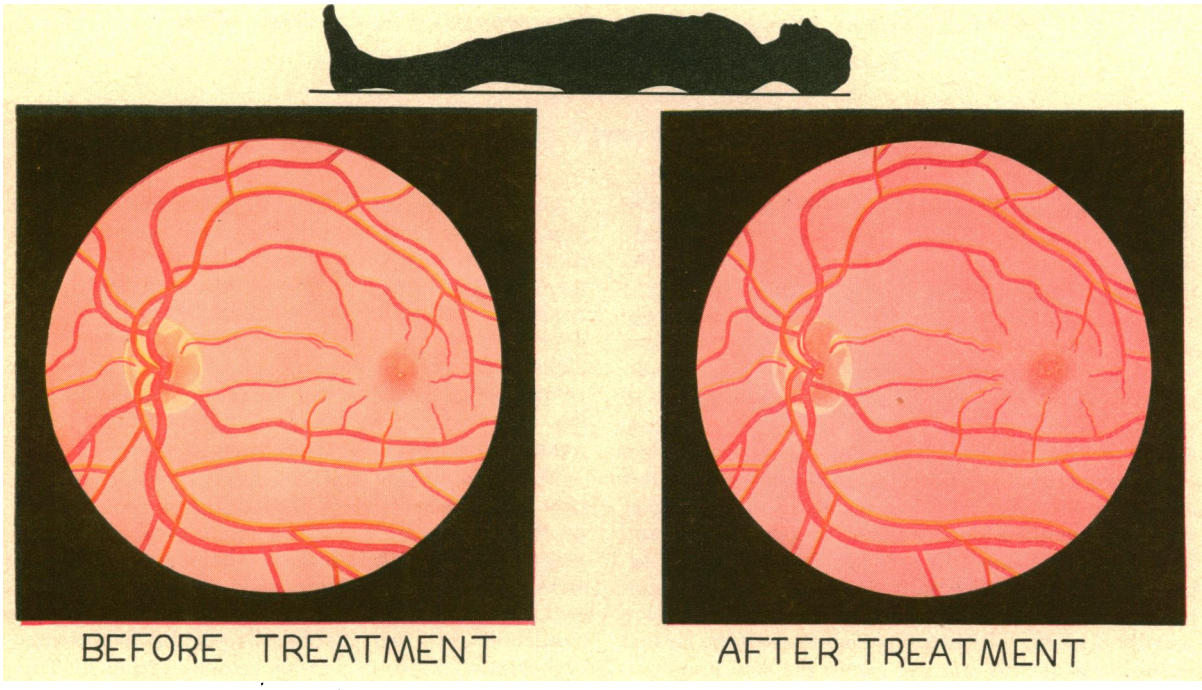
Other studies[7, 10, 11, 14, 21, 22, 28, 30] have suggested that the defect in postural adaptation is not a defect in arteriolar vasoconstriction but rather one in maintenance of adequate return of venous blood to the heart and that this is an essential factor in the production of orthostatic hypotension and orthostatic tachycardia[7, 10, 11, 14, 21, 22, 28, 30]. Failure of venous return produces a marked decrease of the filling of the heart, decreased cardiac output, and, subsequently, diminution of the peripheral pulse.

MacLean, Allen and Magath[22] stress the point that a considerable amount of work has been focused on the nervous influences on the arterial side of the vascular system while the role of the autonomic nervous system in the maintenance of capillary-venous tone has been neglected. They[22] have classified this syndrome into two groups: Group 1—inconsistent orthostatic failure of venous return; group 2—consistent orthostatic failure of venous return. Under group 1 are classified those patients who may or may not demonstrate at any one time the classical signs and symptoms of failure of venous return in the erect posture, namely, weakness, faintness, and occasional syncope, associated with orthostatic hypotension or tachycardia. Both the signs and symptoms disappear in the recumbent position. Usually, no objective evidence of organic dysfunction of the autonomic nervous system can be demonstrated. Group 2 is composed of those patients in whom objective disorders of the autonomic nervous system are common. These patients are those who are suffering from tabes dorsalis, diabetic neuritis, combined sclerosis of pernicious anemia, exophthalmic goitre, diabetes insipidus, disseminated sclerosis, hypopituitarism with chromophobe adenoma, syringomyelia, Adie's syndrome, myosthenia gravis, Addison's disease, and sprue. To this group belong, also, those patients who have undergone extensive sympathectomy for hypertension and who have a consistent orthostatic defect of venous return for a variable period after operation.

Minor grades of circulatory disturbances may be seen in effort syndrome and convalescence following infectious diseases.

The treatment of orthostatic hypotension has consisted of various mechanical procedures such as tight abdominal and leg binders and the "head-up" sleeping position, the avoidance of any type of strenuous exertion on warm days and the use of various vasoconstrictors as well as an increased oral intake of salt and small doses of desoxycorticosterone[5, 6, 7, 8, 12, 13, 15, 17, 18, 27]. Efforts to find a satisfactory remedy for orthostatic hypotension have been disappointing.

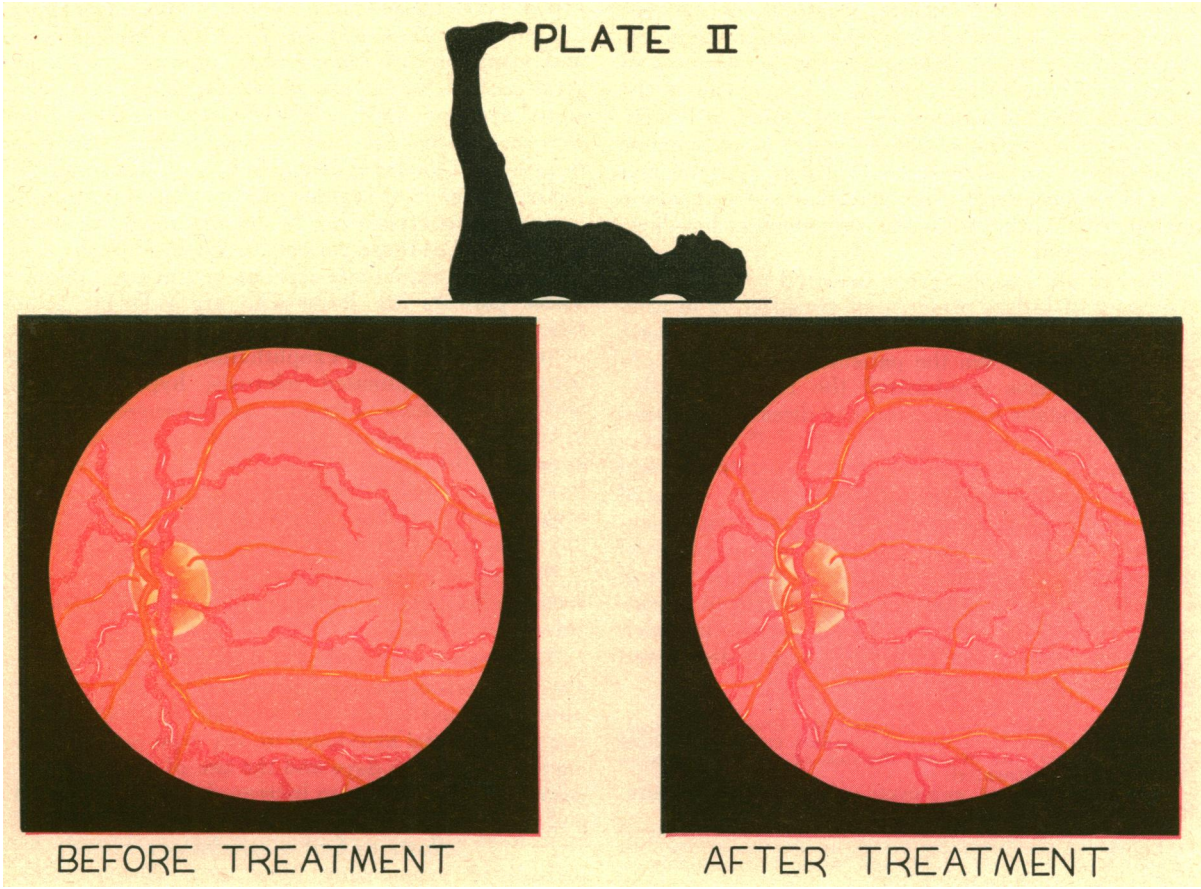
PLATE I



BEFORE TREATMENT

AFTER TREATMENT

PLATE II



BEFORE TREATMENT

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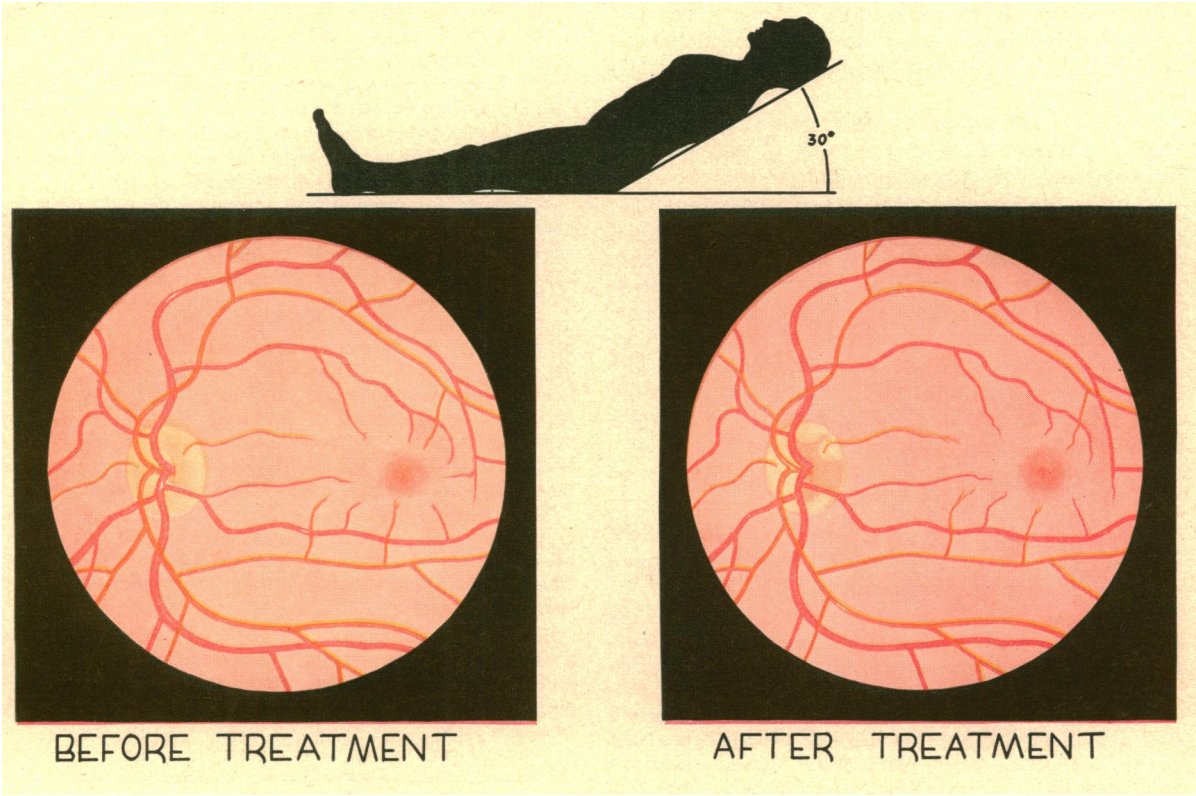
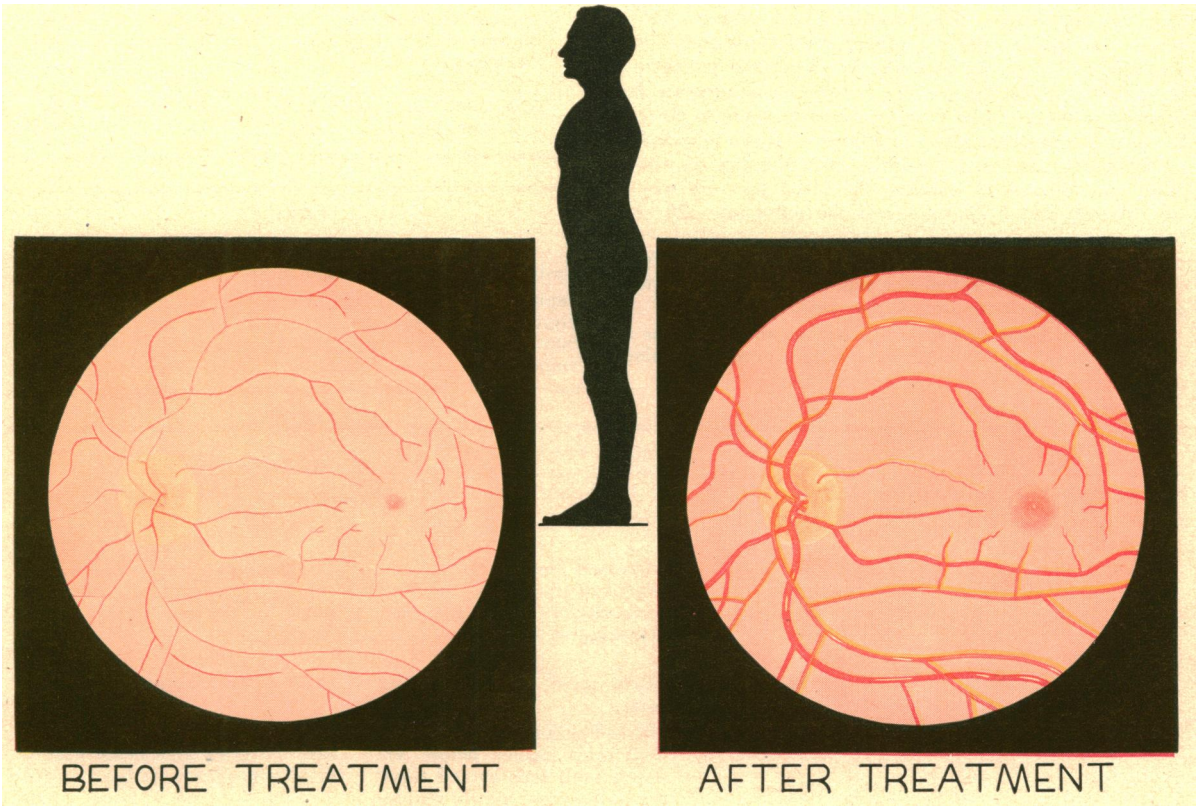


PLATE IV



This is especially true of sympathomimetic or vasoconstricting drugs. Usually the dosage of paredrine used had been small and the beneficial results only temporary.

Since wide variations of blood pressure, heart rate and symptoms may occur, a study of patients who have orthostatic hypotension requires careful control with regard to external temperature, hydration of the body, and the intervals between feedings. Clinical observations under controlled conditions are presented on four patients who had marked, consistent defects of venous return. The effect of the postural state on the vascular pattern of the retinal vessels and the cardiac rhythm is demonstrated. The effect on the venous return by a single large oral dose of paredrine is shown. The treatment has been symptomatic and no claim to a cure is made.

CASE REPORT

The following case report demonstrates the effect of posture on the retinal vascular pattern, venous pressure, and circulation time:

A white man, diabetic, aged 23 years, entered the Los Angeles County General Hospital on August 20, 1946, complaining of diarrhea, numbness of his lower extremities, impotence, marked weakness, dizziness, severe headache with blurring of vision and occasionally syncope which occurred after getting out of bed in the morning. The patient stated that he had to lie down to obtain relief, that his symptoms were much worse in the morning and that he progressively improved as the day advanced. The patient perspired lightly over his face and neck and was intolerant to heat.

Pallor and a dry, scaly skin were noted in the general physical examination of the patient, who appeared much younger than his stated age. The brachial blood pressure in the supine position was 105 mm. of mercury systolic and 75 mm. diastolic, and the pulse rate was 86. When the patient had been erect for one minute the systolic blood pressure had dropped to 80 mm., the diastolic blood pressure to 68 mm., the pulse rate had increased to 96 and he began to complain of weakness, dizziness, headache and blurring of vision. After two minutes of standing the blood pressure was 30 mm. systolic and 0 diastolic, and the pulse rate 120; and before the pulse rate could be taken again, the impulses became very feeble and rapid and the patient collapsed. After the patient had been in bed in a supine position for one minute, almost all the symptoms disappeared.

The carotid sinus syndrome was absent and there was no clinical evidence of Addison's disease. Pulse rate and blood pressure readings are summarized in Table 1.

The venous pressures and the circulation times as determined by using 20 per cent sodium decholin, studied in the various positions are shown in Table 2.

The retinae were studied to determine if changes in the vascular pattern occurred with changes in posture. Interesting changes, not previously described, were observed and these observations are shown in Table 3 and in the colored plates made from paintings of the fundi.

Ephedrine was given at first in treating the orthostatic hypotension, but no improvement was noted. Paredrine was administered in doses of 20 to 60 mgm. four times a day without much effect. Since the symptoms occurred immediately after the patient arose in the morning, it was decided to use a large single dose of paredrine, orally, 30 to 60 minutes before he got out of bed. Paredrine was administered in single doses as high as 200 mgm. without any undesirable reactions, and a dose of 160 mgm. was finally found to be effective. After the administration of paredrine the patient did not complain of marked weakness, severe headache, dizziness or blurring of vision and syncope did not occur. The patient was then able to be up and about for the remainder of the day.

Before treatment with paredrine, the blood pressure would drop to about 30 mm. of mercury systolic and 0 diastolic, whereas after the use of paredrine the lowest recording was 70 mm. systolic and 40 mm. diastolic. Other effects noted are shown in Table 4.

Course: This patient took 160 mgm. of paredrine, daily, in a single dose, orally, for four and one-half months with complete relief of symptoms and without toxic effects. It was impossible to follow him for a longer period, as he moved away from this area.

TABLE 1

Position	Blood Pressure	Pulse
Supine	105/75	84
Supine with legs elevated	120/80	80
Supine at 30° angle	90/50	94
Standing:		
1 min.	88/68	96
2 min.	30/ 0	110
3 min.	0/ 0	120 to?

TABLE 2

Position	Circulation Time Arm-Tongue in Seconds	Venous Pressure MM. Water
Supine	18	0°—65
Supine with legs elevated	12	
Supine at 30° angle	20	45°—78
Standing	26	90°—88

TABLE 3.—*Retinal Vascular Patterns*

Position	Blood Pressure	Pulse	Before Treatment	After Treatment
Supine	110/60	84	Normal.	Normal.
Supine with legs elevated	120/80	80	Increased redness disc and fundus, marked distention and tortuosity of veins and less streaking of arteries.	Slight to moderate distention veins. No apparent change noted in arteries.
Supine at 30° angle	90/50	94	Slight pallor of disc, smaller veins.	No apparent change.
Standing	50/20 30/0	96-120	Marked pallor of disc and fundus, veins empty before arteries, both arteries and veins are narrow and faintly visible.	Slight pallor of disc and fundus. Arteries and veins well filled and clearly visible.

TABLE 4—*Blood Pressure*

Position	Treatment Before	After
Supine	105/75	110/80
Supine with legs elevated	120/80	116/80
Supine at 30° angle	90/50	110/80
Standing	30/ 0	80/60-90/65
Pulse		
Supine	86	84
Supine with legs elevated	82	88
Supine at 30° angle	94	86
Standing	120	90

CASE REPORT

The following case is similar to the first one and demonstrates the effect of posture upon the retinal vascular pattern and the effective control of venous return with paredrine:

A woman, aged 37, complained of dizziness, blurred vision, weakness, headache and faintness of two years' duration. The carotid sinus syndrome was absent and general physical examination disclosed no abnormality. The brachial blood pressure in the supine position was 108 mm. of mercury systolic, 80 mm. diastolic, and the pulse rate was 72. In the supine position with the legs elevated the blood pressure was 128 systolic, 78 diastolic and the pulse rate 80. With the patient in the erect position, at the end of two minutes the blood pressure was 80 systolic, 58 diastolic, the pulse rate 100 and the patient became very weak, dizzy and almost collapsed. The effects of posture upon the vascular pattern of the retina were similar to those observed in the first case described. Paredrine, orally, in a single daily dose of 100 mgm. 45 minutes before arising has controlled this patient's symptoms.

CASE REPORT

The following report illustrates a typical case of orthostatic hypotension in which effective control was not obtained with the administration of divided doses of paredrine but was achieved after a large single dose was administered:

A man, aged 55 years, complained of dizziness, weakness, dimness of vision and headache of several years' duration. The carotid sinus syndrome was absent. No abnormality was noted upon general physical examination. The blood pressure in the supine position was 110 mm. of mercury systolic, 76 mm. diastolic, and the pulse rate was 76. With the patient in the supine position with the legs elevated, the blood pressure was 122 mm. systolic, 80 mm. diastolic, and the pulse rate was 80. With the patient in the erect position, after three minutes of standing, the blood pressure was 84 mm. systolic, 60 mm. diastolic and the pulse rate 100. Paredrine, 40 mgm. three times a day and then every four hours, did not improve the patient's condition but when it was given in a single daily dose of 100 mgm. orally, 30 minutes before the patient arose, the symptoms were controlled effectively.

CASE REPORT

The following report of a typical case of orthostatic hypotension demonstrates the effect of posture on cardiac rhythm. This observation has not been previously described:

A physician, aged 52 years, had known that he had orthostatic hypotension with the usual symptoms and a postural cardiac arrhythmia for many years. The carotid sinus syndrome was absent and no abnormality was noted upon general physical examination. The blood pressure in the supine position was 104 mm. of mercury systolic and 70 mm. diastolic, and the pulse rate was 78. In the supine position with the legs elevated the blood pressure was 122 mm. systolic, 80 mm. diastolic, pulse rate 76. With the patient in the erect position, at the end of two minutes the blood pressure was 74 mm. systolic, 50 mm. diastolic, and the pulse rate 110. The electrocardiographic tracings (Figure 1) showed the onset and offset of arrhythmia due to the effect of posture. The tracings showed a change from normal sinus rhythm to premature contractions of auricular and ventricular origin to auricular fibrillation on assuming the erect position. The reverse was true when the patient assumed the supine position with the legs elevated. The blood pressure rose to normal (122 mm. systolic, 80 mm. diastolic) with a pulse rate of 76, and the arrhythmia reverted to normal sinus rhythm. Paredrine in a single daily dose of 140 to 160 mgm. taken orally one hour before arising in the morning controlled this patient's symptoms and arrhythmia.

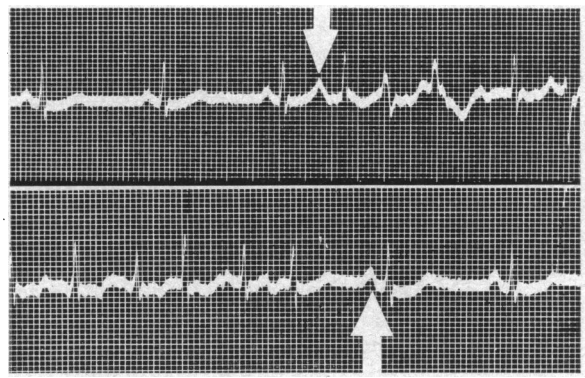


Figure 1. Above, Onset; Below, Offset.

COMMENT

It appears that the essential factor in the syndrome of orthostatic hypotension and orthostatic tachycardia is the failure of return of an adequate amount of venous blood to the heart. This defect of venous return becomes evident in a very short time after the patient stands; conversely, adequate circulation, a normal heart rate and blood pressure follow the resumption of a supine position.

The cause of this disorder appears to be generalized abnormally low venous capillary tone. In the syndrome of orthostatic hypotension, pooling of abnormal quantities of blood occurs caudad as the patient assumes the erect position and the elimination of this syndrome occurs when the pool of blood is shifted cephalad either with or without elevation of the lower extremities with the patient in the supine position. However, when the legs are elevated the syndrome is eliminated sooner. Because of this pooling of blood, with the patient in the erect position, failure of normal venous return occurs, resulting in anoxia with its signs and symptoms.

New clinical evidence to support this view is strongly suggested by the following observations:

1. With the patient in the supine position, elevation of the legs produces an increased hyperemia with distention and tortuosity of the retinal vessels, slight elevation in blood pressure, slight decrease in pulse rate and a shortened circulation time. When the legs are lowered, with the patient still in the supine

position, the retinal vessels become smaller in diameter, producing a decreased hyperemia of the retinae. With the patient in the upright position, the reverse occurs and the circulatory defect as seen in the retinae is marked and is characterized by pallor of the disc and fundus due to the decreased amount of blood in the retinal vessels with an associated drop in blood pressure, increased pulse rate and venous pressure and a prolonged circulation time. Resumption of the supine position abolishes these phenomena.

2. The effect upon the heart is shown by the abnormal cardiac rhythm and by the depression of the S-T segments in the electrocardiogram. The mechanism responsible for these changes is due to the decreased venous return to the heart and the resulting anoxia of the myocardium. Wiggers[29] states that pathological studies suggest that localized interference with the natural blood supply is one of the most common factors. Special regions of the nodal and conducting tissue are supplied with individual coronary artery branches, experimental ligation of which almost invariably leads to disturbances of conduction or rhythm. Katz[16] states that in electrocardiograms of a patient with orthostatic hypotension, there may be S-T-T changes on the patient's assuming the upright position and that these changes disappear if the standing posture is maintained. Such changes were not noted in patients observed by the author of this presentation.

The mechanism responsible for the maintenance of normal capillary venous tone or postural vascular adaptation is not fully understood. Because of the apparent absence of this tone, a sympathomimetic drug, without any central action, relatively non-toxic and safe in large doses, 100 to 200 mgm., orally, was used at a time when it was most needed with the hope that it would increase, by its vasopressor effect, the capillary-venous tone, thereby increasing the venous return to the heart and would maintain this action in a manner approaching normal and long enough for the normal mechanism to take over. It is felt from the observations presented herein that these effects were obtained.

CONCLUSION

1. New observations in the vascular pattern of the retinae in the syndrome of orthostatic hypotension and orthostatic tachycardia are reported for the first time.

2. New observations of cardiac arrhythmia, myocardial ischemia and injury in the electrocardiographic pattern in orthostatic hypotension are reported for the first time.

3. Further clinical observations are reported as evidence that possibly the cause for this syndrome is generalized abnormally low venous-capillary tone in the body.

4. Paredrine is a safe sympathomimetic drug and should be administered in an amount sufficient to produce the desired pharmacological and physiological effects.

5. In four cases orthostatic hypotension and orthostatic tachycardia were successfully treated with a single, daily, oral dose of paredrine hydrobromide.

Note: Since this paper was prepared eight more patients with orthostatic hypotension have been studied with similar findings and results, but none of the patients showed cardiac arrhythmia or ischemia.

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Bronchial Asthma in Infants and Children—Its Diagnosis and Treatment

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BRONCHIAL asthma in early and late childhood as in adult life[3] and old age[4] is practically always due to food or inhalant allergy or both, rarely to drug and bacterial allergy. This conclusion is based on the demonstrated causes in 156 infants and young children up to the age of five years and in 255 older children up to the age of 15 years observed between 1940 and 1946, in whom good or excellent results have been obtained. These results compare with those in similar age groups published in 1937.[10]

In this series, asthma occurred twice as frequently in males as in females (Table 1), whereas in later age groups the males and females were equal in number. There was a familial predisposition to asthma in 50 per cent of the cases with a lesser tendency to other manifestations of allergy. As noted in Table 2, moderate or moderately severe symptoms of asthma were most common. The frequency of other manifestations of allergy is also shown, perennial nasal allergy occurring in 56 per cent.

TABLE 1.—*Number of Patients, Males and Females, and Family History of Possible Allergy*

	Age of Child 0-5 Years	5-15 Years	Totals
Number of Patients	156	255	411
Males	102	174	276
Females	54	81	135
Family History:			
Bronchial Asthma	84	125	209
Nasal Allergy	68	67	135
Headaches	14	28	42
Eczema	9	16	25
Hives	8	10	18
Gastrointestinal Symptoms	8	20	28

DETERMINATION OF ALLERGIC CAUSES OF BRONCHIAL ASTHMA

I. HISTORY

The history is more important than skin testing. This is recorded in all our patients according to a previously published plan.[5,8]

A. Evidence Indicating Food Allergy

1. Bronchial asthma due to food allergy may begin at any time of life, even in old age.

TABLE 2.—*Duration and Degree of Bronchial Asthma and Occurrence of Other Manifestations of Allergy*

Duration of Asthma (in years):	Age of Child 0-5 Years (156 Cases)	5-15 Years (255 Cases)	Totals
0- 1	73	35	108
1- 2	52	29	81
2- 5	31	77	108
5-10	....	98	98
10-15	....	16	16
Degree of Asthma:			
Mild	20	15	35
Moderate	43	79	122
Severe	76	130	206
Very Severe	17	31	48
Other Manifestations:			
Nasal Allergy			
(a) Perennial	92	165	257
(b) Spring to Winter	8	25	33
Hives	21	22	43
Eczema	71	84	155
Headaches	3	13	16
Gastrointestinal Symptoms	16	41	57